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09/672,126	09/27/2000	Gunther Hartmann	CI039/7044 (AWS)	6887
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EXAMINER				
NGUYEN, QUANG				
ART UNIT		PAPER NUMBER		
1636				
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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/672,126

**Applicant(s)**

HARTMANN ET AL.

**Examiner**

Quang Nguyen, Ph.D.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 47,122,143,159 and 201 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-10,18-24,65,82,103,202-214,216-227,230-243,245-257 and 259-263 is/are allowed.
- 6) ☒ Claim(s) 176, 266, 268-276 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

Continuation of Disposition of Claims: Claims pending in the application are 1-10,18-24,47,65,82,103,122,143,159,176,201-214,216-227,230-243,245-257,259-263,266 and 268-276.

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### **DETAILED ACTION**

Applicant's amendment filed on 7/26/04 has been entered.

Amended claims 1-10, 18-24, 47, 65, 82, 103, 122, 143, 159, 176, 201-214, 216-227, 230-243, 245-257, 259-263, 266 and 268-276 are pending in the present application.

This application contains claims 47, 122, 143, 159 and 201 drawn to an invention nonelected with traverse in the Response to Restriction dated 3/25/02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Amended claims 1-10, 18-24, 65, 82, 103, 176, 202-214, 216-227, 230-243, 245-257, 259-263, 266 and 268-276 are examined on the merits herein.

### ***Response to Amendment***

The rejection under 135 USC 102(b) as being anticipated by Krieg et al. (WO 96/02555) is withdrawn in light of Applicants' amendment.

The obviousness-type double patenting rejection as being unpatentable over claims 1-2 of U.S. Patent No. 6,429,199 in view of Siegel et al. (Science 184:1835-1837, 1999) is withdrawn in light of Applicants' amendment.

The provisional obviousness-type double patenting rejection as being unpatentable over claims 1-2, 6, 11-13, 16 and 18 of the copending Application No. 10/017,995 is withdrawn in light of Applicants' amendment.

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### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on January 26, 2004 has been considered by Examiner. However, there is no attached PTO-1449.

### ***Claim Objections***

Claim 175 is objected to because the term "IPCs" should be spelled out completely at the first occurrence of the term in an examined claim. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended claims 176, 266 and 268-276 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method of stimulating production of a plurality of type I interferon subtypes in a mammalian subject comprising administering to a mammalian subject in need of IFN- $\alpha$  treatment an amount of immunostimulatory nucleic acid effective to induce natural interferon-producing cells (IPCs) to secrete at least two type I interferons, wherein said immunostimulatory nucleic acid is selected from the group recited in claim 176, does not reasonably provide enablement for the method as claimed in any other subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make and/or use the invention commensurate in scope with these claims.

***This is a new ground of rejection necessitated by Applicants' amendment.***

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The instant specification is not enabled for the present broadly claimed invention for the reasons discussed below.

***(a) The breadth of the claims.*** The claims encompass a method of stimulating production of a plurality of type I interferon subtypes in any subject including any vertebrate such as a fish, a frog as well as a mammal (see instant specification, page 30, lines 10-8) using an amount of immunostimulatory nucleic acid effective to induce natural interferon-producing cells (IPCs) to secrete at least two type I interferons, wherein said immunostimulatory nucleic acid is selected from the group recited in claim 176.

***(b) The state and the unpredictability of the prior art.*** At the effective filing date of the present application (9/27/1999), little was known on the immune responses in vertebrate species such as a fish or a frog, let alone on the specific induction of natural interferon-producing cells (IPCs) to secrete at least two type I interferons to any significant level by the recited immunostimulatory nucleic acids to yield the desired

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treatment results contemplated by Applicants. There is no evidence in the prior art at the effective filing date of the present application or in the present disclosure that non-mammalian subjects contain any interferon producing cell population that can be stimulated or induced by the immunostimulatory nucleic acids of the present invention. Furthermore, there is no evidence of record indicating or suggesting the presence of a cell population functionally equivalent to the human immature plasmacytoid dendritic cells (pDC), the major IFN- $\alpha$  producing cell being activated by the immunostimulatory nucleic acid of the present invention, in species such as fish or frog or numerous other non-mammalian vertebrate species. It is further noted that the physiological art is recognized as unpredictable (MPEP 2164.03).

*(c) The amount of direction or guidance presented.* Apart from the exemplification showed that certain CpG oligonucleotides such as ODN 1585 (ggGGTCAACGTTGAgggggG, SEQ ID NO:1), ODN 2216 (ggGGGACGATCGTCgggggG, SEQ ID NO:7), all of which contain at least one CG dinucleotide in a palindromic sequence and a poly-G sequence at each end, are capable of inducing plasmacytoid dendritic cells (pDC), the principle type I interferon producing cells in human blood and a critical effector cell type of the immune system for antiviral and antitumor responses (Siegal et al., Science 284:1835-1837, 1999, IDS), to produce IFN- $\alpha$ , the instant specification fails to provide sufficient guidance for a skilled artisan on how to use the immunostimulatory nucleic acid as recited in claim 176 to stimulate production of a plurality of type I interferon subtypes in any other non-mammalian subject to attain the desired results contemplated by Applicants, particularly

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the subject is in need of IFN- $\alpha$  treatment (e.g., increasing efficacy of IFN- $\alpha$  treatment, decreasing a dose of IFN- $\alpha$  effective for treatment, reducing an IFN- $\alpha$  treatment related side effects). Given the general state of the art as discussed above, coupled with the lack of sufficient guidance provided by the present application it would have required undue experimentation for a skilled artisan to make and use the method as broadly claimed.

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issue set forth above, the unpredictability of the physiological art in general, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

### ***Conclusions***

***Claims 1-10, 18-24, 65, 82, 103, 202-214, 216-227, 230-243, 245-257 and 259-263 are allowed.***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP



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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (571) 272-0767, or SPE, Irem Yucel, Ph.D., at (571) 272-0781.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (703) 872-9306.**


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

*Quang Nguyen, Ph.D.*

  
DAVID GUZE  
PRIMARY EXAMINER